

Applicant : Graeme Semple, et al.  
Serial No. : 10/560,332  
Filed : September 8, 2006  
Page : 2 of 8

Attorney's Docket No.: 22578-004US1 / 059.US2.PCT

1. The present application is the U.S. National Stage of International Application No. PCT/US2004/018389, filed on June 10, 2004. As such, the present application is subject to unity of invention practice in accordance with 37 CFR 1.475 and 1.499 (see MPEP § 1896). 37 CFR 1.475 provides as follows:

a) An international and a national stage application shall relate to one invention only or to a group of inventions so linked as to form a single general inventive concept ("requirement of unity of invention"). Where a group of inventions is claimed in an application, the requirement of unity of invention shall be fulfilled only when there is a technical relationship among those inventions involving one or more of the same or corresponding special technical features. The expression "special technical features" shall mean those technical features that define a contribution which each of the claimed inventions, considered as a whole, makes over the prior art.

(b) An international or a national stage application containing claims to different categories of invention will be considered to have unity of invention if the claims are drawn only to one of the following combinations of categories:

- (1) A product and a process specially adapted for the manufacture of said product; or
- (2) A product and process of use of said product; or
- (3) A product, a process specially adapted for the manufacture of the said product, and a use of the said product; or
- (4) A process and an apparatus or means specifically designed for carrying out the said process; or

(5) A product, a process specially adapted for the manufacture of the said product, and an apparatus or means specifically designed for carrying out the said process.

(c) If an application contains claims to more or less than one of the combinations of categories of invention set forth in paragraph (b) of this section, unity of invention might not be present.

(d) If multiple products, processes of manufacture or uses are claimed, the first invention of the category first mentioned in the claims of the application and the first recited invention of each of the other categories related thereto will be considered as the main invention in the claims, see PCT Article 17(3)(a) and § 1.476(c).

(e) The determination whether a group of inventions is so linked as to form a single general inventive concept shall be made without regard to whether the inventions are claimed in separate claims or as alternatives within a single claim.

2. MPEP § 1850 III. B. provides as follows for determining unity of invention in "the situation involving the so-called Markush practice:"

The situation involving the so-called Markush practice wherein a single claim defines alternatives (chemical or non-chemical) is also governed by PCT Rule 13.2. In this special situation, the requirement of a technical interrelationship and the same or corresponding special technical features as defined in PCT Rule 13.2, shall be considered to be met when the alternatives are of a similar nature.

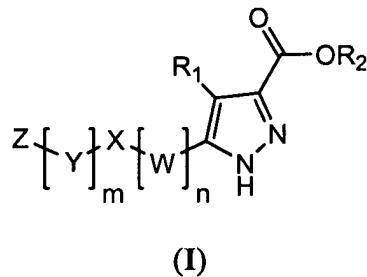
When the Markush grouping is for alternatives of chemical compounds, they shall be regarded as being of a similar nature where the following criteria are fulfilled:

- (A) All alternatives have a common property or activity; and
- (B)(1) A common structure is present, i.e., a significant structural element is shared by all of the alternatives; or
- (B)(2) In cases where the common structure cannot be the unifying criteria, all alternatives belong to a recognized class of chemical compounds in the art to which the invention pertains.

In paragraph (B)(1), above, the words "significant structural element is shared by all of the alternatives" refer to cases where the compounds share a common chemical structure which occupies a large portion of their structures, or in case the compounds have in common only a small portion of their structures, the commonly shared structure constitutes a structurally distinctive portion in view of existing prior art, and the common structure is essential to the common property or activity. The structural element may be a single component or a combination of individual components linked together.

3. This response is being filed concurrently with a Supplemental Amendment, which instructs the Office to amend independent claims 1 and 178 as follows:

A compound of Formula (I):



wherein:

W and Y are independently is a straight or branched chain C<sub>1-5</sub> alkylene group optionally containing one double bond[[,]] or one triple bond or carbonyl, wherein said C<sub>1-5</sub> alkylene group is optionally substituted with halogen, hydroxyl, C<sub>1-4</sub> alkyl, C<sub>1-4</sub> haloalkyl or C<sub>1-4</sub> alkoxy;

Y is a straight or branched chain C<sub>1-5</sub> alkylene group optionally containing one double bond, or one triple bond or carbonyl, wherein said C<sub>1-5</sub> alkylene group is optionally substituted with halogen, hydroxyl, C<sub>1-4</sub> alkyl, C<sub>1-4</sub> haloalkyl or C<sub>1-4</sub> alkoxy;

X is -NR<sub>3</sub>C(O)-, -C(O)NR<sub>3</sub>, -NR<sub>3</sub>S(O)O<sub>2</sub>-, -S(O)O<sub>2</sub>NR<sub>3</sub>-, -NR<sub>3</sub>C(O)NR<sub>4</sub>-, -NR<sub>3</sub>C(O)O-, -OC(O)NR<sub>3</sub>-, -NR<sub>3</sub>-, -C(O)-, -CH(OH)-, -C(NH)-, -O-, -S-, -S(O)- or -S(O)<sub>2</sub>-;

R<sub>3</sub> and R<sub>4</sub> are independently H, C<sub>1-4</sub> alkyl, phenyl or heteroaryl, wherein each of said alkyl, phenyl and heteroaryl are optionally substituted with 1 to 5 substituents selected from the group consisting of halogen, hydroxyl, thiol, cyano, nitro, C<sub>1-4</sub> haloalkyl, amino, C<sub>1-4</sub> alkylamino, di-C<sub>1-4</sub>-alkylamino, C<sub>1-4</sub> alkyl, C<sub>1-4</sub> alkoxy, C<sub>2-4</sub> alkenyl, C<sub>2-4</sub> alkynyl, C<sub>1-4</sub> haloalkoxy, C<sub>1-4</sub> alkylthio, C<sub>1-4</sub> alkylsulfinyl, C<sub>1-4</sub> alkylsulfonyl, C<sub>1-4</sub> haloalkylthio, C<sub>1-4</sub> haloalkylsulfinyl and C<sub>1-4</sub> haloalkylsulfonyl;

Z is H, halogen, phenyl or heteroaryl, wherein said phenyl and heteroaryl are optionally substituted with 1 to 5 substituents selected from the group consisting of halogen, hydroxy, thiol, cyano, nitro, C<sub>1-4</sub> haloalkyl, amino, C<sub>1-4</sub> alkylamino, di-C<sub>1-4</sub>-alkylamino, C<sub>1-4</sub> alkyl, C<sub>1-4</sub> alkoxy, C<sub>2-4</sub> alkenyl, C<sub>2-4</sub> alkynyl, C<sub>1-4</sub> haloalkoxy, C<sub>1-4</sub>

alkylthio, C<sub>1-4</sub> alkylsulfinyl, C<sub>1-4</sub> alkylsulfonyl, C<sub>1-4</sub> haloalkylthio, C<sub>1-4</sub> haloalkylsulfinyl and C<sub>1-4</sub> haloalkylsulfonyl;

R<sub>1</sub> is H, hydroxyl, halogen, C<sub>1-4</sub> alkyl or C<sub>1-4</sub> haloalkyl;

R<sub>2</sub> is H or C<sub>1-8</sub> alkyl and

"n" and "m" are each ~~independently 0 or 1~~;

4. Independent claims 1 and 178 as presently amended now require that both "m" and "n" must each be "1" (i.e., W and Y in formula (I) must both be present). As such, restriction groups **I-IX** are now moot because each of Groups **I-IX** is directed to compounds in which one or both of "m" and "n" is "0." As such, claims 1 and 178 as presently amended now encompass the subject matter of only three of the twelve originally proposed restriction groups, namely:

Group **X** (m is 1, n is 1, and Z is H or halogen);

Group **XI** (m is 1, n is 1, and Z is phenyl); and

Group **XII** (m is 1, n is 1, and Z is heteroaryl).

As can be seen, each of Groups **X**, **XI**, and **XII** differ only in the identity of variable Z, which is the substituent located at the leftmost (terminal) end of the group attached to the 5-position of the pyrazole ring.

5. Applicants submit that independent claims 1 and 178 should be examined in their entirety-- i.e., Groups **X**, **XI**, and **XII** should be rejoined and examined in concert in the present application-- because the Markush group recited in each of claims 1 and 178 meet the PCT unity of invention criteria for Markush practice as set forth in MPEP § 1850. This is discussed in more detail below.

A. The Markush group recited in each of claims 1 and 178 as presently amended embraces chemical compound alternatives that are of similar nature, i.e., the alternatives share both a common property (e.g., agonists for the RUP25 receptor).

B. The Markush group recited in each of claims 1 and 178 as presently amended embraces chemical compound alternatives that share a significant structural element. More

specifically, the claims require that the pyrazole ring must be substituted at two positions, namely:

- (i) at the 3-position with a carboxylic acid or ester group; and
- (ii) at the 5-position with an alkylene moiety, which itself must be:
  - (a) interrupted with a heteroatom-containing linker (i.e., variable "X");  
and
  - (b) terminated with a hydrogen, halogen, optionally substituted phenyl, or  
optionally substituted heteroaryl<sup>1</sup>.

As can be seen, there is a significant structural commonality among the alternatives of the presently claimed Markush group.

The Markush group recited in each of claims 1 and 178 as presently amended therefore at least meets criteria (A) and (B)(1) for unity of invention as set forth in PCT Rule 13.1 and MPEP § 1850 for Markush practice. Moreover, Applicants' amendments to the claims have, e.g., reduced the number of points of variability in the substituent attached to the 5-position, thereby providing claimed subject matter that can be searched without causing undue burden to the Office.

Applicants respectfully request that the present restriction requirement at least be withdrawn with respect to Groups **X**, **XI**, and **XII** so that the presently amended claims can be examined in their entirety.

6. Applicants also respectfully request that Group **XIII**, claims 179-187, drawn to methods of use of the compounds and compositions as presently claimed in claims 1 and 178, be examined in concert with at least Group X. 37 CFR § 1.475(b)(2) states that a national stage application containing claims to different categories of invention will be considered to have unity of invention if the claims are drawn to a combination of a product and a process of use of said product. Since the claims in group XIII relate to a use of the compounds and compositions recited in, e.g., Group X, these groups of claims have unity of invention with Group X under 37

---

<sup>1</sup> This is by virtue of the fact that the claims now require that both m and n must be 1, and as such, both W and Y must be present.

CFR § 1.475(b)(2). Applicants therefore request reconsideration of this restriction and examination of Groups XIII with at least Group X, XI, and XII.

7. Finally, Applicants wish to address the Office's *a posteriori* determination of lack of unity. The claims as originally filed (and apparently searched by the Office) also required that the 5-position of the pyrazole ring must be a substituent other than hydrogen (i.e., even when m and n are both 0, both variables X and Z must still be present). However, the Office's "preliminary search" did not appear to take this required structural attribute into account. This is evidenced by the fact that the Office's query structure only appeared to provide for substitution at the 1 and 3 positions, but not at the 5-position. Moreover, the provisos at the end of the claim also do not appear to have been considered in the Office's analysis. As such, the Office's "preliminary search" does not appear to provide sufficient basis for a finding of lack of unity.

Applicant : Graeme Semple, et al.  
Serial No. : 10/560,332  
Filed : September 8, 2006  
Page : 8 of 8

Attorney's Docket No.: 22578-004US1 / 059.US2.PCT

### CONCLUSION

Applicants believe the foregoing to be a *bona fide* attempt to provide the Office with a fully responsive reply to the present restriction requirement. Applicants encourage the Examiner to contact the undersigned should the Examiner wish to discuss the restriction groups, this election, or a proposed search strategy.

Enclosed is a check for the Five Month Petition for Extension of Time fee. Please apply any charges or credits to Deposit Account No. 06-1050, referencing Attorney Docket No.: 22578-004US1.

Respectfully submitted,

Date: December 13, 2007

/John T. Kendall/  
John T. Kendall, Ph.D.  
Reg. No. 50,680

Fish & Richardson P.C.  
225 Franklin Street  
Boston, MA 02110  
Telephone: (617) 542-5070  
Facsimile: (617) 542-8906

21806962 (2).doc